## 1-78. (cancelled)

- 79. (currently amended) A vaccine or inoculum comprising an immunogenic effective amount of immunogenic particles dissolved or dispersed in a pharmaceutically acceptable diluent, wherein said immunogenic particles are comprised of a plurality of recombinant chimeric hepatitis B core (HBc) protein molecules in which said recombinant chimeric HBc protein molecules have a length of up to about 515 amino acid residues that
- (a) contain a sequence of at least about 130 of the N-terminal 150 amino acid residues of the HBc molecule that include one or more peptide-bonded heterologous epitopes at the N-terminus, or in the HBc immunogenic loop or a heterologous linker residue for a conjugated epitope present in the HBc immunodominant loop,
- (b) contain one to ten cysteine residues toward the C-terminus [C-terminal cysteine residue(s)] of the molecule from the C-terminal residue of the HBc sequence and within about 30 residues from the C-terminus of the chimer molecule [C-terminal cysteine residue(s)],
- (c) contain a sequence of at least 5 amino acid residues from HBc position 135 through position 140 toward to the HBc C-terminus, and zero to about 100 amino acid residues in a sequence heterologous to HBc from position 150 to the C-terminus,

said chimer molecules containing no more than 20 about 5 percent conservatively substituted amino acid residues in the HBc sequence, and

said particles being substantially free of binding to nucleic acids, and being more stable on storage at 1 mg/mL using 50 mM NaPO<sub>4</sub>, pH 6.8 than are particles formed from an otherwise identical HBc chimer that lacks said C-terminal cysteine residue(s) or in which a C-terminal cysteine residue present in the chimer molecule is replaced by another residue.

- 80. (currently amended) The vaccine or inoculum according to claim 79 wherein said recombinant chimeric HBc protein molecules have a length of about 135 to about 515 amino acid residues and contains four peptide-linked amino acid residue sequence domains from the N-terminus that are denominated Domains I, II, III and IV, wherein
- (a) Domain I comprises about 71 to about 100 amino acid residues whose sequence includes at least the sequence of the residues of position 5 through position 75 of HBc and optionally includes a heterologous epitope containing up to about 30 amino acid residues peptide-bonded to one of HBc residues 1-4:
- (b) Domain II comprises about 5 to about 250 amino acid residues peptide-bonded to HBc residue 75 of Domain I in which (i) at least 4 residues in a sequence of HBc positions 76 through 85 are present peptide-bonded to one to about 245 amino acid residues that are heterologous to HBc and constitute a heterologous epitope or a heterologous linker residue for a conjugated epitope or (ii) the sequence of HBc at positions 76 to 85 is present free from heterologous residues;

- (c) Domain III is an HBc sequence from position 86 through position 135 peptide-bonded to residue 85 of Domain II; and
- (d) Domain IV comprises (i) 5 through fourteen residues of a HBc amino acid residue sequence from position 136 through 149 peptide-bonded to the residue of position 135 of Domain III, (ii) one to ten cysteine residues [C-terminal cysteine residue(s)] within about 30 residues from the Cterminus of the chimer molecule, and (iii) zero to about 100 amino acid residues in a sequence heterologous to HBc from position 150 to the C-terminus, with the proviso that Domain IV contain at least 6 amino acid residues including said one to ten cysteine residues of (ii), said recombinant chimeric HBc protein molecules being more stable on storage at 1 mg/mL using 50 mM NaPO<sub>4</sub>, pH 6.8 than are particles formed from an otherwise identical HBc chimer molecule that lacks said C-terminal cysteine residue or in which a C-terminal cysteine residue present in the chimer molecule is replaced by another residue and having an amino acid residue sequence in which no more than about 5 percent of the amino acid residues are conservatively substituted in the HBc sequence.
- 81. (original) The vaccine or inoculum according to claim 80 that contains a heterologous linker residue for a conjugated epitope in Domain II and further includes a hapten linked to said heterologous linker residue.
- 82. (previously presented) The vaccine or inoculum according to claim 79 wherein said recombinant chimeric HBc

protein molecules have a length of about 175 to about 240 amino acid residues and contain four peptide-linked amino acid residue sequence domains from the N-terminus that are denominated Domains I, II, III and IV, wherein

- (a) Domain I comprises about the sequence of the residues of position 1 through position 75 of HBc;
- (b) Domain II comprises about 5 to about 55 amino acid residues peptide-bonded to HBc residue 75 of Domain I in which at least 4 residues in a sequence of HBc positions 76 through 85 are present peptide-bonded to 6 to about 50 amino acid residues that are heterologous to HBc and constitute a heterologous epitope;
- (c) Domain III is an HBc sequence from position 86 through position 135 peptide-bonded to residue 85 of Domain II; and
- (d) Domain IV comprises (i) 5 through fourteen residues of a HBc amino acid residue sequence from position 136 through 149 peptide-bonded to the residue of position 135 of Domain III, and (ii) zero to about 50 amino acid residues in a sequence heterologous to HBc from position 150 to the C-terminus,

said particles exhibiting a ratio of absorbance at 280 nm to 260 nm of about 1.4 to about 1.6.

- 83. (original) The vaccine or inoculum according to claim 79 that is adapted for parenteral administration.
- 84. (original) The vaccine or inoculum according to claim 79 that is adapted for mucosal immunization.

- 85. (original) The vaccine or inoculum according to claim 79 wherein said recombinant chimeric HBc protein molecule particles are present in an attenuated strain of *S. typhi, S. typhimurium* or a *S. typhimurium-E. coli* hybrid.
- 86. (original) The vaccine or inoculum according to claim 79 wherein said recombinant chimeric HBc protein molecule particles are present in plant tissue.
- 87. (original) The vaccine or inoculum according to claim 79 that further includes an adjuvant.
- 88. (original) The vaccine or inoculum according to claim 87 wherein said adjuvant is alum.
- 89. (original) The vaccine or inoculum according to claim 87 wherein said adjuvant is a small molecule selected from the group consisting of a muramyl dipeptide, 7-substituted-8-oxo- or 8-sulfo-guanosine derivative, monophosphoryl lipid A, aluminum or calcium salts.
- 90. (original) The vaccine or inoculum according to claim 87 wherein said adjuvant is an oil that is emulsified with said immunogenic particles and said pharmaceutically acceptable diluent.
- 91. (original) The vaccine or inoculum according to claim 90 wherein said emulsion is an water-in-oil emulsion having a water phase and an oil phase.

- 92. (original) The vaccine or inoculum according to claim 90 wherein said emulsion is an oil-in-water emulsion having a water phase and an oil phase.
- 93. (original) The vaccine or inoculum according to claim 92 wherein the oil phase of said emulsion comprises squalene.
- 94. (original) The vaccine or inoculum according to claim 92 wherein the oil phase of said emulsion comprises squalane.
- 95. (original) The vaccine or inoculum according to claim 90 wherein the water and oil phases of said emulsion are emulsified by an emulsifying agent that is a sorbitan or mannide  $C_{12}$ - $C_{24}$  fatty acid ester.
- 96. (original) The vaccine or inoculum according to claim 95 wherein said emulsifying agent is a mannide  $\rm C_{12}\text{-}C_{24}$  fatty acid ester.
- 97. (original) The vaccine or inoculum according to claim 96 wherein said  $\rm C_{12}\text{-}C_{24}$  fatty acid of said mannide  $\rm C_{12}\text{-}C_{24}$  fatty acid ester is oleic acid.

## 98-109. (cancelled)

110. (original) A method of inducing an immune response in an inoculated host animal that comprises the steps

of inoculating a host animal with a vaccine or inoculum according to claim 79, and maintaining that inoculated animal for a time period sufficient for that animal to develop an immune response.

- 111. (original) A method of inducing an immune response in an inoculated host animal that comprises the steps of inoculating a host animal with a vaccine or inoculum according to claim 80, and maintaining that inoculated animal for a time period sufficient for that animal to develop an immune response.
- 112. (original) A method of inducing an immune response in an inoculated host animal that comprises the steps of inoculating a host animal with a vaccine or inoculum according to claim 82, and maintaining that inoculated animal for a time period sufficient for that animal to develop an immune response.
- 113. (original) A method of inducing an immune response in an inoculated host animal that comprises the steps of inoculating a host animal with a vaccine or inoculum according to claim 87, and maintaining that inoculated animal for a time period sufficient for that animal to develop an immune response.
- 114. (original) A method of inducing an immune response in an inoculated host animal that comprises the steps of inoculating a host animal with a vaccine or inoculum according to claim 88, and maintaining that inoculated animal

for a time period sufficient for that animal to develop an immune response.

115. (original) A method of inducing an immune response in an inoculated host animal that comprises the steps of inoculating a host animal with a vaccine or inoculum according to claim 92, and maintaining that inoculated animal for a time period sufficient for that animal to develop an immune response.